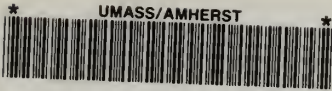


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AN EPIDEMIOLOGIC INVESTIGATION OF
REPRODUCTIVE HEALTH AMONG EMPLOYEES
AND OF CHILD HEALTH AMONG PUPILS
AT THE INDIAN BROOK ELEMENTARY SCHOOL,
PLYMOUTH, MASSACHUSETTS

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A Report
of the

DIVISION OF FAMILY HEALTH SERVICES
MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

October 28, 1982

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School nurses at Plymouth Elementary Schools

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DEFINITIONS

Adverse (poor) reproductive outcome:	A pregnancy which ends in a less than optimal result, including miscarriages, stillbirths, congenital malformations, low-birth weight, and neonatal deaths.
Agent:	Suspected cause of an outcome of illness.
Ambient:	Surrounding, pertaining to the general environment in which an organism functions.
Association:	A connection between two events. It says nothing about what causes what.
Carcinogen:	Any cancer-producing substance.
Confidence interval:	A technical term that means approximately: The range within which the value obtained would be expected to fall a specified percentage (usually 95%) of the time if repeated sampling and calculating of the same situation were done.
Congenital anomaly:	A mental or physical anomaly which exists at birth; may be hereditary, or due to some influence during gestation. (ICDA 9 Codes 740-760).
Epidemiology:	The study of the distribution of disease in human populations and of the factors that determine that distribution.
Etiology:	The cause of disease.
Fetal death:	A death prior to the complete expulsion or extraction from its mother of a fetus, irrespective of the duration of pregnancy. See stillbirth and miscarriage.
Follow-up study:	A study in which groups of individuals are defined on the basis of their <u>exposure</u> status. May be either prospective or retrospective.
Gestation:	The period of pregnancy.
Gravidity:	Number of pregnancies.
Hypothesis:	An idea. All scientific and statistical tests are designed to disprove hypotheses. When the tests fail to do so, credence, but not proof, is lent to the idea.
Incidence/incidence rate:	Number/or rate of <u>newly</u> occurring cases in defined place and time.
Infant mortality:	Death to a live born child during first year of life.

Miscarriage:	Death to a fetus before 20 weeks of gestation.
Mutagenic:	Having the power to produce mutation.
Mutation:	A change in the character of a gene that is perpetuated in subsequent divisions of the cell in which it occurs.
Neonatal mortality:	Death to a live born child <u>before</u> 28 days of age.
Odds ratio:	A ratio that compares the risk of having a specified outcome if one is exposed to an agent or event versus the risk of having the same outcome if one is not exposed.
Prevalence:	The number of existing cases divided by the number of persons (both ill and well) in a population at a specified point in time.
Probability:	A quantitative description of chance. In statistics, 95% probability is usually used.
Rate:	Number of occurrences per population or per a specified time period.
Relative risk:	An epidemiologic statistic that compares the true risks for a given outcome in different populations; it is approximated by calculating an odds ratio.
Retrospective:	Describes a study in which the disease has occurred among subjects before the study starts.
Significance/statistical significance:	A technical term used in statistics. It means that the comparison being made takes into account and corrects for the roles of chance and random variation. Saying that there is no significant difference between two different numbers means that the observed difference can be due to chance.
Spontaneous abortion:	See miscarriage.
Sterility:	Failure to conceive or cause conception. Usually a specified period of 12-24 months is used.
Stillbirth:	A death to a fetus of 20 or more weeks gestation or greater than 350 grams prior to complete expulsion from its mother.

Teratogen:

A drug or other agent that causes abnormal fetal development.

Teratogenic:

Causing abnormal fetal development.

I. INTRODUCTION

In July, 1982, the Division of Family Health Services (DFHS), was asked by the Division of Environmental Health Assessment to assist in responding to concerns about an increased number of poor reproductive outcomes among teachers at the Indian Brook Elementary School (IBES), Plymouth, MA. Mr. Richard O'Keefe, Director of Health and Sanitation, Plymouth, had requested that the Division of Environmental Health Assessment and the Massachusetts Department of Environmental Quality Engineering undertake an examination of the school environment to determine whether or not hazardous materials were present.*

As DFHS began its assessment of the reproductive outcomes, additional concerns became apparent about an unusually high number of childhood cancers and about increases in headaches, dizziness, nausea, and respiratory symptoms among students. The key question raised was: Was the environment at IBES responsible for causing these poor reproductive outcomes, childhood cancers, and illnesses? The two environmental agencies as well as an independent toxicology consultant investigated whether or not hazardous exposures were present. DFHS assumed responsibility for investigating whether or not the reported illnesses and outcomes were higher than would be expected. The purpose of this report is to present the findings of the investigation and explain these findings to the community.

*Suspected high rates of cancers were reported by the Town of Plymouth during the summer of 1981. DEHA determined that the number of cases at that time was within normal expected ranges.

II. SUMMARY OF ENVIRONMENTAL INVESTIGATIONS AT

INDIAN BROOK ELEMENTARY SCHOOL

The Indian Brook Elementary School, with a current enrollment of 658 students, is located in the Manomet area of Plymouth, Massachusetts. The school was first occupied in February, 1977. An addition containing five classrooms was completed in November, 1978. The school was designed for energy efficiency and has a closed environment. All ventilation is provided via the Heating, Ventilation, and Air Conditioning System (HVAC). IBES is one of four "new" buildings which were constructed using the same design within a short period of time. In response to concerns that the IBES might be contaminated with hazardous chemicals, a thorough environmental investigation was conducted by various agencies. The Massachusetts Department of Environmental Quality Engineering (DEQE) and the U.S. Environmental Protection Agency (EPA) tested the drinking water at IBES for the presence of 129 "Priority Pollutants" as defined by EPA, pesticides, volatile organics, and heavy metals, and bacteria. These tests were all negative.

The Massachusetts DEQE and Cambridge Analytical Associates, a private laboratory, conducted tests on soil and run-off water samples obtained near and under the school. No hazardous chemicals were present in either soil or run-off samples.

Some concern was raised about the possibility of radiation exposure. Since 1980, the Division of Radiation Control, Massachusetts Department of Public Health, has maintained a radiation measurement device one quarter of a mile from the IBES. Radiation measurements have never exceeded background levels during this time.

The Massachusetts Division of Occupational Hygiene (DOH) and the U.S. National Institute of Occupational Safety and Health (NIOSH) inspected the ventilation system at IBES. Both agencies recommended that fresh air intake be increased to 15 cubic feet per minute per student. NIOSH found that the control modules on the HVAC system were not calibrated to deliver the indicated amount of fresh air and that "essentially no fresh air was admitted unless the dial was set at 30% or greater."

Various tests on air samples were taken inside the school by DOH, NIOSH, and by Cambridge Analytical Associates. Tests for total hydrocarbons, carbon monoxide, and nitrogen dioxide were negative. Formaldehyde levels ranged from 0.05 to 0.09 parts per million (ppm) with the ventilation system off and 0.02 to 0.03 ppm with the ventilation on. It is generally agreed that 0.1 ppm is an acceptable level for indoor air.

Formaldehyde is a colorless, flammable gas with a strong, suffocating, pungent odor. As an important industrial chemical of major commercial use, formaldehyde is found throughout the environment, in homes as well as in the workplace. Formaldehyde resins are used in particle board, plywood, thermal insulation, hardware, home appliances, most textiles, and carpentry.

Other products which contain formaldehyde are cosmetics, pharmaceuticals, paper, and paint. It is thought that the formaldehyde levels found at IBES are the result of out-gassing from the wooden cabinets.

The first signs or symptoms noticed on exposure to formaldehyde at concentrations ranging from 0.1 to 5 ppm are burning of the eyes, lacrimation (tearing), and general irritation to the upper respiratory passages. Higher exposures (10-20 ppm) may produce coughing, a sensation of tightening in the chest, a sense of pressure in the head, gastric disturbances, visual disturbances, and palpitation of the heart.

Recent studies have shown formaldehyde to cause nasal and lung cancer in experimental animals at levels of 14 ppm. A computerized literature search failed to find studies that describe any effects of formaldehyde on reproduction.

Levels of formaldehyde found at Indian Brook Elementary School are less than those which produce symptoms discussed above and much less than levels which produced cancer in animals. Of course, it is always desirable to keep exposures to a minimum. Fresh air flow at rates recommended by the Department of Labor and Industries, Division of Occupational Hygiene, should substantially decrease formaldehyde levels.

Methanol was used as a duplicating fluid in the teachers' lounge at Indian Brook Elementary School. The duplicating machine, which is similar to others used in many schools and businesses, was in fairly constant use--several hours during the day. Methanol (methyl alcohol) was not found in the air samples taken by DOH since the duplicating machines had not been in operation since late June. NIOSH personnel conducted tests for potential methanol exposure while two duplicating machines were operating. Based on the results of these tests, NIOSH determined that people operating the duplicating machines may be exposed to excessive methanol levels after only four minutes of continuous operation. Other staff in the teachers' lounge would also be exposed to methanol while the machines were in use.

Methanol, which is a colorless liquid, is used in paints, varnishes, cements, inks, and dyes. Toxicity can result from ingestion, skin absorption, or inhalation of methanol. Most toxicology studies are concerned with health effects of methanol ingestion. Symptoms due to ingestion include: headaches; weakness; vertigo; nausea, and vomiting; vision defects, including blindness, and respiratory distress progressing to convulsions and sometimes death.

While hundreds of cases of poisoning due to ingestion have been reported, there are very few studies regarding toxic effects due to methanol inhalation. One study found office workers exposed to fumes from duplicating machines had recurrent headaches and sore throats. Another report concerned workers exposed to methanol fumes in a sheepskin dyeing factory complaining of persistent headache, dizziness, and irritability. Evidence suggests that chronic exposure to 1,200 to 8,300 ppm can lead to impaired vision. Other signs and symptoms of methanol intoxication include dizziness and behavioral disturbances; concentrations in excess of 20 ppm may lead to recurring headache.

Symptoms which may result from inhalation (breathing in) methanol, at

levels measured in the teachers' lounge at IBES, include headaches, fatigue, and irritability. A computerized literature search revealed that there are no studies of reproductive effects of methanol exposure in animals or humans. Some other sources of methanol exposure are exhaust from vehicles fueled by methanol-gasoline mixtures; cigarette smoke; and certain foods, including Brussel sprouts, celery, and onions.

Due to the malfunction of the ventilation system, it appears that during the months of February, March, and April, 1982, fresh air was changed only once every 18 hours instead of the expected rate of three changes per hour. It is very likely that lack of sufficient fresh air contributed to headaches, dizziness, and symptoms of tiredness reported by children and staff at the IBES.

The following reports were prepared by the environmental agencies which conducted testing at the IBES and by Toxicon, a toxicology consulting firm independently hired by the Plymouth School Committee, and are the basis of the information discussed in this section:

1. Indian Brook School Health Problems Progress Report No. 3, Toxicon Associates, Natick, MA, October 4, 1982.
2. U.S. Department of Commerce, National Technical Information Service, NTIS -- Water-Related Environmental Fate of 129 Priority Pollutants. Volume I: Introduction and Technical Background, Metals and Inorganics, Pesticides and PCB's, prepared for Environmental Protection Agency, Washington, D.C., December, 1979.
3. U.S. Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio, 45226. Indian Brook Elementary School, Plymouth, Massachusetts, Interim Report No. 1, HETA 82-372, September, 1982.
4. Massachusetts Department of Environmental Quality Engineering - Bacteriological Analysis Report, September 9, 1982.
5. Massachusetts Department of Labor and Industries, Division of Occupational Hygiene Report, September 13, 1982.

III. A REVIEW OF THE LITERATURE ON ENVIRONMENTAL INFLUENCES ON REPRODUCTIVE HEALTH

Advances in synthetic chemistry in recent years have resulted in an increasingly complex chemical environment. As environmental and occupational exposures increase in frequency and complexity, medical and public health assessment of the health impact of these agents and the establishment of environmental control mechanisms becomes increasingly complicated.

Approximately one hundred thousand chemicals are in relatively common use, and more than two thousand new chemicals are introduced each year. Most have not been tested for their capacity to be mutagenic (causing changes in genes), carcinogenic (causing cancer), or teratogenic (causing abnormal fetal development). What testing has been done has been conducted on animal models. Thus, generalization to humans is severely limited.

While people of all ages are at risk from potential health hazards of chemicals, the developing fetus is particularly sensitive. Because the placenta is permeable to essentially everything taken into the mother, the fetus is exposed to multiple agents. Abnormalities in germ cells caused by exposure of males and females prior to pregnancy may result in either infertility or adverse reproductive outcomes. Exposures prior to and during pregnancy may lead to miscarriage, stillbirth, congenital malformation, increased incidence of cancer in offspring, or developmental delays. The purpose of this brief section is to review what is known about environmental influences on reproductive health.

At the present time, five percent of all liveborn infants in the United States have significant congenital disease or birth defects. However, while the etiology of most cases is unknown, it is estimated that about twenty-five percent are due to genetic or chromosomal abnormalities and ten percent are attributable to environmental agents. In addition, miscarriage occurs in fifteen to twenty-five percent of recognized pregnancies, and stillbirth occurs at a frequency of two to four percent of total births. Most adverse reproductive outcomes have not been attributed to a particular etiologic agent. This is true for a number of reasons. Many anomalies are of multifactorial etiology, meaning that they have a genetic as well as environmental or other components. There may be combined effects from two or more agents. A single agent may give rise to different effects depending upon dose and time of exposure. For example, radiation produces a continuum of effects depending on the stage of gestation during which exposure takes place. Very early exposure apparently has an "all or nothing" effect. High dose exposure during the period of rapid brain development is associated with microcephaly and mental retardation. Third trimester exposure is related to low birth weight and neonatal mortality. Because we are exposed to numerous agents, it is extremely difficult to determine which factor is responsible. A second reason is related to health care delivery patterns which allow physicians to see only a small segment of the population, therefore, preventing the easy identification of a cluster. In addition, data on the incidence of specific anomalies are inaccurate due to incomplete reporting on birth certificates. Data on miscarriages are even more limited as there currently is no mandatory reporting mechanism in place.

For all of these reasons, one can see that failure to detect effects should not be misconstrued as proof of no association. Exposure to environmental chemicals can be classified into three major groups: occupational, ambient, and exposure through consumer products. Occupational reproductive health hazards occur in the workplace where concentrations of certain chemicals reach much higher levels than in the general environment.

Ambient exposures affect the largest numbers of people. The major sources of ambient pollution are industrial effluents and automobile exhaust. Common pollutants include sulfur dioxide, nitrogen oxides, carbon monoxide, ozone, lead, cadmium, and unburned hydrocarbons. Carbon monoxide, ozone, cadmium and lead have all been implicated in adverse reproductive outcomes. Fetal, neonatal and infant deaths have been reported in association with air pollution. Ambient exposures take place through intake of contaminated water and air and consumption of contaminated plant and animal products. Once chemicals are in the food chain they are difficult to eliminate. Most exposures through consumer products are to drugs, tobacco, alcohol, hair dyes, cosmetic products, and food additives such as preservatives, saccharin, and red dye number two. Indirect food additives include chemicals used to promote weight gain and antibiotic residues found in meat and dairy products.

A number of chemicals have been strongly associated with adverse reproductive outcomes. Wives of men occupationally exposed to vinyl chloride monomer (VCM) and to chloroprene appear to be at increased risk for fetal loss. Numerous studies have reported association between exposure to anesthetic gases and adverse reproductive effects for male and female operating room personnel.

Pesticides are a subject of increasing concern regarding their potential carcinogenic and adverse reproductive effects. The National Institute for Occupational Safety and Health recently concluded that there were eight pesticides, including aldrin, dieldrin, endrin and 2,4,5-T for which there were sufficient data suggesting that they may be teratogenic in humans. Thousands of Vietnamese and Americans were exposed to the defoliant 2,4,5-T, also known as "Agent Orange", which was contaminated with dioxin. During the early 1970s, large quantities of 2,4,5-T were also sprayed on forests in Oregon. An EPA study demonstrated that there was an increased incidence of spontaneous abortions during peak spraying periods. Breast milk of women in this study contained significant concentrations of dioxin. Both 2,4,5-T and dioxin are known animal teratogens, but there is no conclusive evidence concerning their teratogenicity in humans. Kepone and dibromochloropropane (DBCP) have been shown to cause decreased fertility or sterility in male pesticide production workers. The accidental discharge of kepone into the James River at Hopewell, Virginia, resulted in contamination of the Chesapeake Bay and subsequent closure of fishing grounds.

Several heavy metals are associated with adverse reproductive outcomes. In Minamata, Japan, pregnant women who ate mercury contaminated fish gave birth to children with severe central nervous system disorders. Mercury also is suspected to cause miscarriage, stillbirth, and neonatal death. Another heavy metal, lead, crosses the placenta and is associated with spontaneous abortion, premature delivery, and stillbirth. Evidence as to whether lead is teratogenic in humans is conflicting. However, lead has been shown to cause chromosomal abnormalities in human spermatozoa.

Effects of radiation on fertility, embryogenesis, and fetal development are well known. Large doses can produce mutations in germ cells and during pregnancy cause fetal abnormalities, mental retardation, miscarriage, and low birthweight. An absorbed dose of ten rads by the fetus is considered to be the threshold for induction of congenital anomalies. Exposures to ionizing radiation in the nuclear industry and medical field do not generally approach levels that have been proven teratogenic. However, exposure to greater than average background levels of radiation results in high rates of chromosomal breakage in lymphocytes. Although it has not been conclusively determined, in utero exposure to less than two rads may result in a two-fold increase in childhood leukemia.

Since the thalidomide tragedy, there has been considerable interest in the role of drugs in the etiology of human malformations. Most pregnant women in the U.S. take five or more drugs. Very few drugs other than thalidomide have been definitely implicated as human teratogens. Folic acid antagonists, such as methotrexate, and the alkylating agents busulphan and cyclophosphamide, are known human teratogens. Currently available evidence suggests that lithium is a likely teratogen. Oral anticoagulants, and warfarin in particular, are associated with fetal hemorrhage and malformations.

Oral contraceptives taken in early stages of an unrecognized pregnancy have been associated with a significantly increased incidence of limb reduction deformities and cardiovascular defects. Androgens and some progestogens can cause virilization of a female fetus. The delayed carcinogenic effect of diethylstilbestrol (DES) on daughters of women taking the drug is well established. In addition to carcinomas, fifty percent of DES daughters have developed benign abnormalities and other structural changes in their reproductive organs. DES has also been associated with urinary tract abnormalities in sons of DES mothers.

Children of epileptic mothers have an increased incidence of malformations, primarily cleft lip and palate, cardiac, skeletal and central nervous system abnormalities. Specific abnormalities are associated with particular anti-convulsants. Diabetic mothers treated with oral hypoglycemics may have a three-fold higher incidence of fetal loss than those receiving diet therapy or insulin. Numerous studies report a significantly increased incidence of malformation, particularly central nervous system and cardiac defects, in offspring of diabetic mothers. Unfortunately, it is not possible to discern whether the excesses of defects are related more closely to diabetes or its treatment.

Excessive alcohol intake during pregnancy is associated with a combination of fetal defects known as the fetal alcohol syndrome, which often includes structural malformations of the heart, face, limbs and bones, mental retardation and intrauterine and postnatal growth deficiency. Moderate consumption of alcohol is associated with miscarriage; daily consumption may be associated with decreased birthweight.

Considerable evidence exists that smoking during pregnancy has a powerful adverse effect upon the well-being of the fetus and subsequent development of

the child. Smoking is associated with increased incidence of miscarriage, bleeding disorders during pregnancy, spontaneous rupture of the membranes, stillbirth, premature birth, and neonatal death.

Intrauterine infections, most of which are viral, may result in congenital malformations, mental retardation, and infant and fetal death. As many as fifty percent of fetuses infected with rubella develop manifestations such as eye lesions, hearing defects, skin and skeletal lesions, and general growth and psychomotor retardation. Cytomegalovirus, toxoplasma gondii, listeria bacillus, genital mycoplasma, herpes simplex, and syphilis are other infectious organisms which are associated with congenital anomalies, stillbirth, fetal death, and miscarriage.

A number of other factors have been associated with adverse reproductive outcomes. Pregnancies subsequent to prior miscarriage are generally recognized to be at higher risk for prematurity and fetal death. This risk probably decreases with increasing gravidity. Several research groups have suggested that miscarriage, particularly of chromosomally normal fetuses is more common in women with a history of prior induced abortion. However, two recent large investigations have concluded that there is no association between prior induced abortions and subsequent miscarriages.

Advanced maternal age, especially after 40, is a generally recognized risk factor for adverse reproductive outcome, including miscarriage, stillbirth, neonatal death, and congenital defects. The increase in Down Syndrome conceptions with increased maternal age is well documented in livebirths as well as in miscarriage. Many common congenital anomalies exhibit significant racial variation. Other factors which have been associated with adverse reproductive outcomes are poor nutrition and low socioeconomic status.

Infertility, the inability to achieve pregnancy after one year of regular, unprotected intercourse, is experienced by ten to fifteen percent of the population of childbearing age. Fifty percent of infertility factors are seen in women; thirty to forty percent are seen in men. For ten to twenty percent of all infertile couples, there appears to be no explainable cause for infertility. In women some factors associated with infertility are diabetes, cardiac disease, various metabolic disorders, and anovulation (lack of ovulation) due to drastic weight gain or loss or emotional stress. Gynecological disorders such as endometriosis, fibroid tumors, and hormonal and anatomical problems can also be responsible for female infertility. Factors which affect male fertility include impotency, varicocele (varicose spermatic vein), sperm antibodies, oligospermia (few sperm), azoospermia (no viable sperm), as well as abnormal sperm morphology. Some causes of male infertility are testicular injury, mumps, sexually transmitted diseases, increase in scrotal temperature, radiation, and alcohol or marijuana use.

Tables III-1 through III-5 and Figure III-1 portray some of the information discussed above in summary form.

Table III-1
FREQUENCY OF SELECTED REPRODUCTIVE END POINTS

<u>EVENT</u>	<u>FREQUENCY (%)</u>
Azoospermia (number, morphology, and motility)	2-3% of men
Failure to conceive after one year of unprotected intercourse	10-15% of couples
Spontaneous abortion (Miscarriage) 8-20 weeks of gestation	15-25% of recognized pregnancies
Stillbirth	2-4% of total births (stillbirths and livebirths)
Congenital malformations	4-5% of liveborn infants
Chromosomal anomalies	30-40% of spontaneous abortions 5% of stillbirths 0.2% of liveborn infants
Low birth weight	7% of liveborn infants

Table III-2

MATERNAL RISK FACTORS:

SPONTANEOUS ABORTION, BIRTH DEFECTS,
AND LOW BIRTH WEIGHT

AGE	DRUGS
GRAVIDITY	ALCOHOL
PREVIOUS SAB	SMOKING
CHROMOSOMAL ABNORMALITIES	DIETHYLSTILBESTROL
RACE - ETHNIC GROUP	UTERINE DISORDERS
SOCIOECONOMIC GROUP - EDUCATION	NUTRITIONAL DEFICIENCY
ACUTE SYSTEMIC DISEASE	HYPERTHERMIA
INFECTIONS	ENVIRONMENTAL EXPOSURES
FEBRILE ILLNESS	
CHRONIC SYSTEMIC DISEASE	OCCUPATION
DIABETES	UTERINE ENVIRONMENT PRIOR TO
ENDOCRINE DISORDERS	WOMAN'S OWN BIRTH
IMMUNOLOGICAL FACTORS	HEREDITARY FACTORS
ABO INCOMPATIBILITY	
CHROMOSOMAL ABNORMALITIES	

Table III-3

PATERNAL RISK FACTORS:

SPONTANEOUS ABORTION AND BIRTH DEFECTS

AGE

OCCUPATION

ACUTE INFECTION

CHROMOSOMAL ABNORMALITIES

DRUGS (ANTICONVULSANTS)

ENVIRONMENTAL EXPOSURE (MOSTLY INFERTILITY)

Figure III-1

CRITICAL PERIODS OF DEVELOPMENT (BLACK DENOTES HIGHLY SENSITIVE PERIODS)

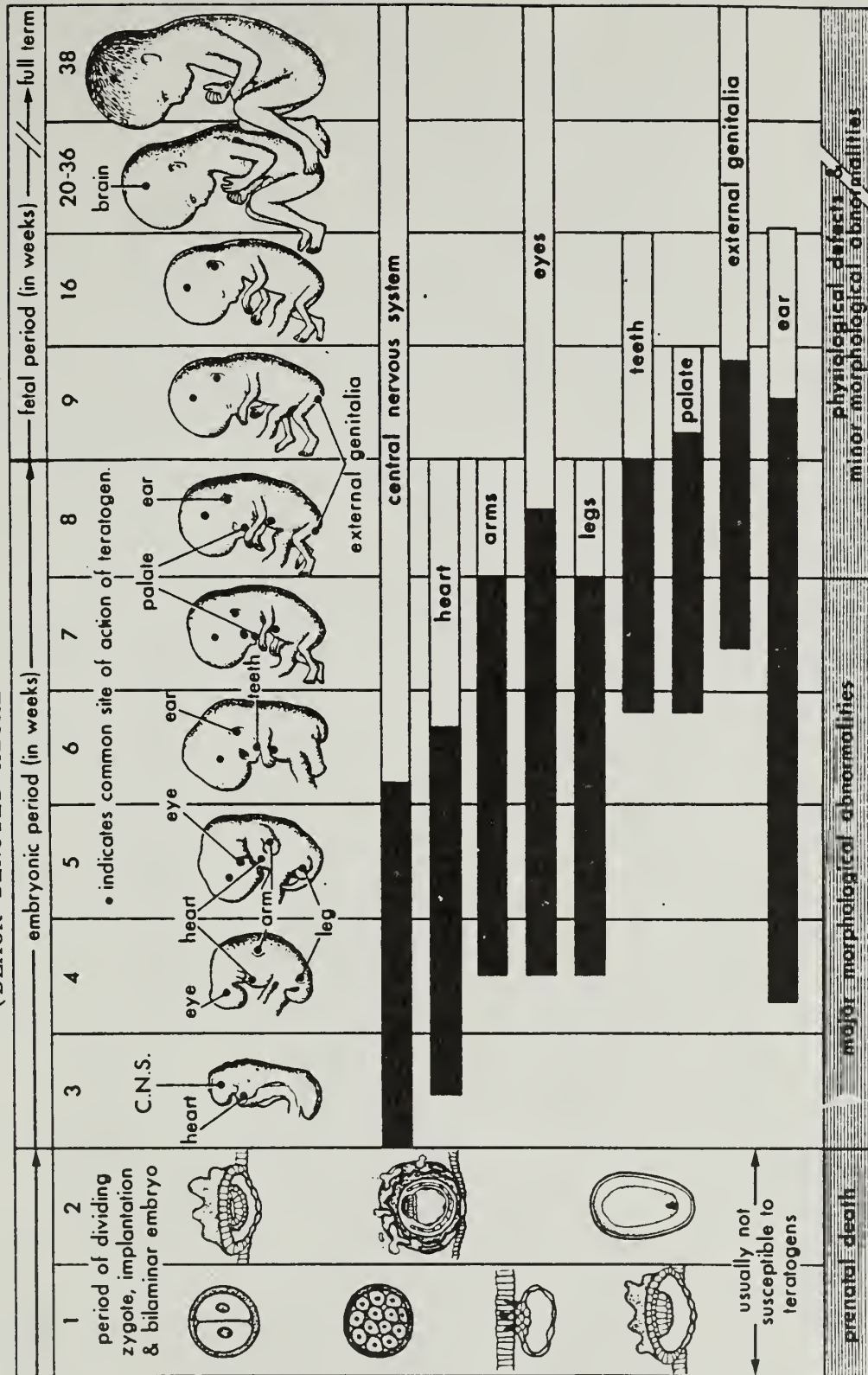


Table III-4

KNOWN HUMAN TERATOGENS

THALIDOMIDE

FOLIC ACID ANTAGONISTS

ALKYLATING AGENTS

METHYL MERCURY

ALCOHOL

DILANTIN

TRIMETHADIONE

WARFARIN (COUMADIN)

TOBACCO

DIETHYLSTILBESTROL

HYPERTHERMIA

LITHIUM

Table III-5

POSSIBLE HUMAN TERATOGENS

RADIATION (DOSE AND TIME DEPENDENT)

ORGANIC SOLVENTS

CARBON MONOXIDE

OZONE

LEAD

CADMIUM

DIOXIN

POLYVINYLCHLORIDE (PVC)

VINYL CHLORIDE MONOMER (VCM)

ANESTHETIC GASES

ALDRIN

DIELDRIN

ENDRIN

2,4,5-T

KEPONE

DIBROMOCHLOROPROPANE (DBCP)

POLYCHLORINATED BIPHENYLS (PCBs)

POLYBROMINATED BIPHENYLS (PBBs)

ANDROGENS

PROGESTOGENS

IV. METHODS OF INVESTIGATION AND ANALYSIS

The main goal of an epidemiologic investigation is to determine an association between one or more events or agents and a specific disease or effect. In the case of the Indian Brook Elementary School the question is whether or not any substances in the school environment resulted in a) poor reproductive outcomes, b) cancer, and/or c) headaches, dizziness, and nausea.

METHODS OF INVESTIGATION

The first step in determining an association is to establish the existence of a result or effect. At IBES, the first task was to establish whether or not the three outcomes listed above were in fact occurring more often than in the general population. The second step in an investigation is to establish the existence of the suspected agent(s) or event(s). One way to do this was to examine the school for the presence of substances known or suspected of being harmful. A second approach was to consider the school itself as the possible agent. In other words, for the purpose of an analysis, the school could be considered the exposure in the absence of any specific, hazardous, identifiable condition or agent. In the course of this investigation both approaches were taken.

The third step in establishing an association is to examine whether the agent and the effect are linked. This linkage is in practice very difficult to both measure and prove. Specific factors that must be considered include:

- 1) Strength of association: the measure of the differences in the effect or outcome in exposed individuals compared to unexposed individuals.
- 2) Consistency of the findings: how often have these effects been linked in other studies or situations involving different populations?
- 3) Specificity of the effect: is this effect known to be linked to a number of other agents, or is the agent related to more than one outcome? (The more possible combinations, the more difficult it is to determine causation.)
- 4) Temporality: did the exposure to the agent precede the event in question?
- 5) Dose Response: do increases in the exposure correspond to increases in the effect? Does reduction or elimination of exposure result in a decrease in the outcome?

- 6) Biological plausibility: is there any biologic mechanism known to explain how the agent could have led to the effect?
- 7) Coherence: does the suggested cause seriously conflict with the generally known facts of the natural history, biology, and epidemiology of the outcome? Is this association similar to other known associations?

The process by which an epidemiologic investigation attempts to determine such relationships can be divided into three levels: Level I, Level II, and Level III.

A Level I investigation is based on easily accessible, routine records. It will usually be carried out with speed and economy and will seldom involve case examinations or special questionnaires (although clinical confirmation of supposed 'cases' is not excluded). Sophisticated studies and medical examinations/testing are not usually carried out. The basic analysis at this level will compare observed rates to expected rates or to rates in other, unexposed populations.

The types of data that are used typically for a Level I investigation include birth rates, infant mortality rates, neonatal mortality rates, fetal death rates, and other types of measures computed from the information contained in official birth and death certificates and population estimates. In addition, available summary records of health status or related data from private and governmental agencies and existing registries of specific illnesses or conditions are also utilized. Individual hospital and medical records may be used to confirm reported diagnoses.

A Level II investigation involves a detailed examination of individuals who are known to have either the exposure or the effect, or both. Ideally, an identical investigation is conducted on a comparison population. The investigation can include the administration of questionnaires, review of an individual's medical and hospital records, and, sometimes, physical examinations, laboratory tests, or other diagnostic procedures. This level also can involve a detailed search for the suspected agents and their distribution.

Finally, a Level III investigation is used to follow over a long period of time a population in which a serious exposure is suspected or confirmed.

The investigations conducted by the Division of Family Health Services consisted of Level I and Level II studies. Level I studies were used to look at cancer, childhood mortality, and childhood illness issues. A combination of Level I and II studies was used to examine the issues of adverse reproductive outcomes.

Once data have been collected at each level, a series of statistical analyses are performed in order to measure the presence of the effect, the

degree to which it is present in both exposed and unexposed populations, and whether or not there are other factors present which could cause or explain the effect. The ultimate objective is to measure the degree to which the effect can be attributed to the exposure or agent.

METHODS OF ANALYSIS

Because of the complexity of most situations being examined in epidemiologic investigations, a number of statistical techniques must be used to sort out the effects of various factors and to measure the strength of the associations. The most common numerical indicator of association is called the odds ratio, which is an estimate of the relative risk of having the outcome if you are exposed to the agent compared to the risk of having the same type of outcome if you are not exposed to the agent. This can also be described as being the rate in exposed persons divided by the rate in nonexposed persons. It is calculated from the following type of chart.

ODDS RATIO			
<u>SUSPECTED CAUSE</u>	<u>DISEASE</u>		TOTAL
	Present	Absent	
Present	a	b	a + b
Absent	c	d	c + d
Total	a + c	b + d	
ratio = $\frac{ad}{cb}$			

An odds ratio of 1.0 indicates that the outcome is no more common in the exposed population than in the unexposed population.

Statistical power is an indicator of the reliability of the odds ratio. Statistical power is used to describe the probability that an effect, if present, will be detected. The power of a study is determined by the frequency of the outcome variable in the unexposed population, the size of the effect expected, the acceptable level of statistical significance, and the sample size. In other words, the more common the outcome in the general population the more difficult it is to determine that any increase is not caused by chance and the larger the size of the study population required to determine if the effect truly exists.

Theoretically, odds ratios between 0.0 and 1.0 indicate that the exposure is actually protective; that is, exposed persons are less likely to have the disease or outcome. Odds ratios greater than 1.0 indicate some degree of relative risk for the exposed group.

Calculation of a confidence interval can give a measure of the difficulty of making an inference about the reliability of the odds ratio. The confidence interval, in fact, is the range in which the true odds ratio will

probably fall. The more powerful a study, the more narrow will be the range of the confidence interval. A very wide confidence interval that contains 1.0 will indicate that little can be inferred about the odds ratio because it could indicate protectiveness, no association, or risk. Most statisticians will read this as meaning that no statistical significance can be concluded. When the confidence interval does not contain 1.0, then an association is suspected regardless of the size of the interval. Unless the interval is very narrow, it is difficult to tell whether small increases in the relative risk (odds ratio close to but not equal to 1.0) are due to chance or to the agent in question.

Detailed information about the specific methods, data sources, and analytic techniques used to examine each issue is provided later in this report.

V. HEALTH STATUS INDICATORS FOR PLYMOUTH

In order to examine whether either adverse reproductive outcome or childhood problem rates at IBES are high, it is helpful to look at health data for the town in general. Interest in the town also was raised after the Division of Family Health Services began to investigate reports of adverse reproductive outcomes at IBES because individuals in the town speculated that the problems were not limited to the school. Accordingly, the DFHS analyzed Level I data to obtain a profile of the community and to compare Plymouth rates with expected values for the state and for other populations.

The following analysis will be divided into three sections examining a) childhood deaths; b) childhood cancers; and c) adverse reproductive outcomes (congenital malformations, fetal deaths, and neonatal mortality).

Childhood Deaths

METHODS

Two data sets were examined to complete an assessment of childhood mortality in Plymouth:

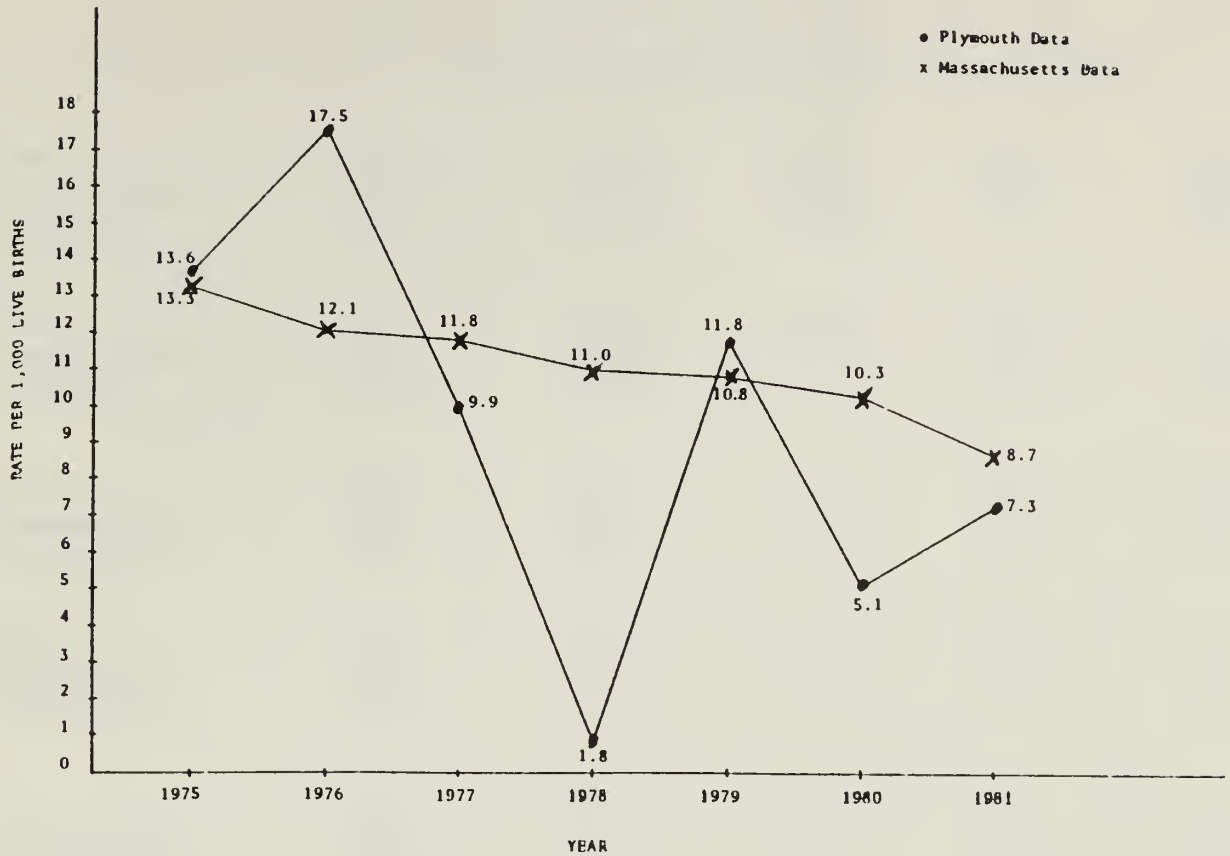
- 1) Infant Mortality Rate, MDPH Vital Statistics
- 2) Childhood Mortality Rate, MDPH Vital Statistics

Both the rates and causes of childhood deaths for Plymouth were reviewed. In response to concerns about possible excessive childhood deaths in certain areas, deaths in the Manomet, Indian Brook, and South school districts were analyzed separately.

FINDINGS

Infant Mortality: The infant mortality rate reflects the health status of children during the first year of life (including neonatal deaths). In Massachusetts, the infant mortality rate has declined from 13.3% in 1975 to 8.7% in 1981. The Plymouth data, as would be expected, tend to show peaks and valleys but do demonstrate an overall decrease from 13.6 in 1975 to 7.3% in 1981. (Figure V-1.) The increase in 1979 reflects an increase in neonatal deaths. The infant mortality rate for Plymouth is not higher than that for all of Massachusetts. Neonatal mortality will be discussed under the sections on reproductive outcomes.

FIGURE V-1.
 INFANT MORTALITY RATE PER 1,000 LIVE BIRTHS IN
 PLYMOUTH AND MASSACHUSETTS (1975 - 1981)



Childhood Mortality: Table V-1 presents a breakdown of childhood mortality rates by age and year for Plymouth, Massachusetts, and the United States. When examining the Plymouth data, it is important to remember that the rates are influenced by small numbers of occurrences. For instance, in the 1-4 age group in both 1976 and 1977, the Plymouth rate is higher than either the Massachusetts or United States rates. A further analysis of the data indicates that 2 deaths occurred in each year, of unrelated causes, and in very different parts of the town. In 1977, for the 15-19 age group, the rate for Plymouth is increased due to 6 accidental deaths. In summary, the data for Plymouth do not demonstrate a higher over-all childhood mortality rate than is seen in Massachusetts or the United States.

The total number of childhood deaths for Plymouth for the years 1975-1980 was 59, ranging from a low of 3 deaths in 1978 to a high of 16 deaths in 1977. As expected, the largest number of the deaths occurred during the first year of life. The second largest number occurred in the 15-19 year age group. Table V-2 presents a summary of these deaths by cause as listed on the death certificate.

TABLE V-1.

CHILDHOOD MORTALITY (per 100,000):
 USA, MASSACHUSETTS, AND PLYMOUTH, 1975-1981

Year	Age at death				
	0 - 1	1 - 4	5 - 9	10 - 14	15 - 19
1975					
USA	1,641	70.8	35.7	35.7	101.5
Massachusetts	1,320	54.7	21.2	26.3	82.8
Plymouth	1,360	58.2	52.8	0	138.8
1976					
USA	1,520	69.9	34.8	34.6	97.1
Massachusetts	1,210	47.0	18.4	21.6	77.9
Plymouth	1,750	120.8	0	93.3	88.2
1977					
USA	1,486	68.8	34.0	35.1	101.6
Massachusetts	1,180	40.2	19.5	24.1	78.6
Plymouth	990	131.7	40.5	0	253.
1978					
USA	1,434	69.2	33.4	34.3	100.9
Massachusetts	1,100	52.4	19.4	23.6	84.9
Plymouth	180	65.7	0	0	40.4
1979					
USA	1,300	NA	NA	NA	NA
Massachusetts	1,080	30.1	19.0	18.9	82.8
Plymouth	510	0	0	33.7	77.5
1980					
Massachusetts	1,043	47.9	19.2	21.3	68.8
Plymouth	518	0	0	30.8	37.2
1981					
Massachusetts	890.8	43.3	22.7	21.2	60.4
Plymouth	690.1	0	30.0	0	74.5
Average, 1975 - 1981					
Massachusetts	1,316	46.5	23.7	24.0	70.7
Plymouth	1,021	41.8	16.5	22.3	95.1

TABLE V - 2

Causes of Death Among Children by Age for
Plymouth Residents, 1975-1980

Cause	Age				
	0-11 months	1-4	5-9	10-14	15-19
Infection		1	1		1
Central Nervous System		2			
Urinary System		1			
Sudden Infant Death Syndrome	3				
Neoplasms					1
Leukemia		1			
Complications of Pregnancy and Childbirth	8				
Immaturity/Prematurity	6				
Respiratory Distress Syndrome	6				
Congenital Anomalies					
Central Nervous System	2				
and neuromuscular					
Cardio-Vascular System	3			1	1
Respiratory	2				
Multiple Anomalies	2				
Accidents		1	1	2	13
TOTALS	32	6	2	3	16

Sixteen out of the 27 deaths during 1975-80 for children ages 1-19 were caused by an accident of some sort. Two deaths were caused by a malignant condition. Twenty of the 32 infant deaths were related to prematurity, respiratory distress syndrome, or complications of pregnancy and childbirth. Nine of the 32 infant deaths were related to a specific congenital anomaly, and two later deaths were the result of congenital heart disease. The examination of the Plymouth data does not indicate that the number of childhood deaths due to cancer or congenital anomalies is above the expected number. Cancer occurrence will be discussed in the next section.

A closer analysis of the deaths from the Indian Brook School district showed that three of the four deaths to children over 10 were related to accidents and one to a congenital anomaly. Of two deaths for the 1-4 age group, one was related to an accident and one to leukemia. The seven infant deaths were due to prematurity (5), respiratory distress syndrome (1), and unspecified congenital anomaly (1). A review of these deaths does not indicate any association between specific cases.

In summary, the examination of infant and childhood deaths revealed no evidence of increased rates for Plymouth. The patterns of causes of childhood deaths is the same as that for the rest of the state. These conclusions are meant to be an overview of health status in Plymouth. The categories used, however, may not be the most sensitive indicators of environmental influences. Therefore, specific studies of cancer and adverse reproductive outcomes were undertaken.

Childhood Cancer

METHODS

Because a large proportion of cancer is now thought to be related to environmental exposures, the incidence of all cancers in children was evaluated. With the assistance of the Massachusetts Cancer Registry, a search was made for all cases of cancer occurring in children ages 0 to 19, who resided in Plymouth from 1975 through the present. Four sources provided data: Jordan Hospital, Sidney Farber Cancer Institute, Plymouth pediatricians, and MDPH Vital Statistics. All cases found were verified and cross-checked to avoid duplicate counting. Cases provided by Plymouth residents were checked against these data sources. A comparison was made with Connecticut, which has had a formal cancer registry for the same time period.

FINDINGS

Fourteen cases of cancer were found; using Plymouth population and age distributions, 12.2 cases of cancer would be expected. Utilizing a statistical procedure (the Poisson distribution for small numbers and rare events), 14 is not statistically different from 12.2 ($p = 0.09$). Of the 14 cases, one occurred in a student at IBES. No statistical evaluation can be made of this single case. Though there were other children at IBES who are known to have cancer, these children developed cancer before entering the school.

Adverse Reproductive Outcomes

METHODS

Frequencies of congenital malformations were obtained from birth certificates and verified from hospital records in questionable cases. Frequencies of fetal and neonatal deaths were obtained from death certificates. Birth and death certificates were obtained from MDPH Vital Statistics.

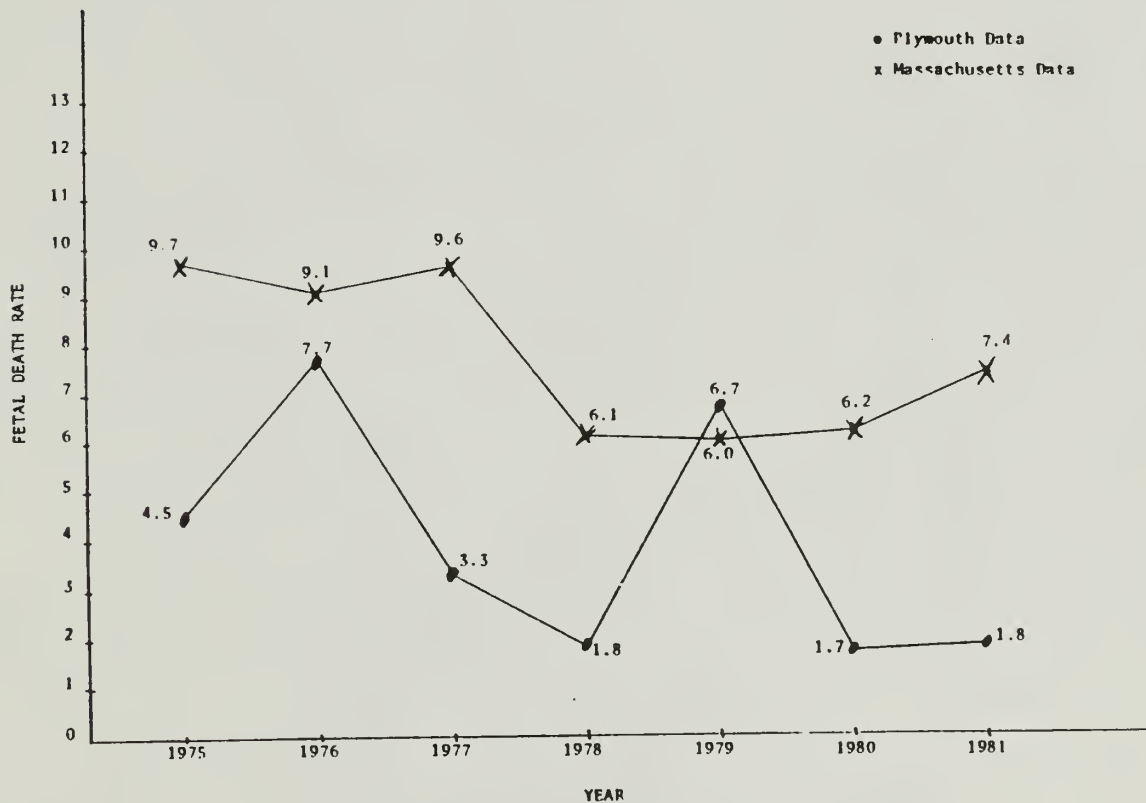
FINDINGS

Congenital Malformations: From 1975 to 1981, 30 Plymouth infants were reported, on their birth certificate, to have a congenital malformation. These include 6 cardiovascular, 5 urinary tract, 4 multiple unspecified, 3 limb, 3 musculo-skeletal, 2 respiratory, 2 ear, face, neck, 2 upper alimentary tract, and one each of skin, central nervous system, and genital anomalies. In summary, 30 out of 3,846 live births were reported to have congenital anomalies, which is 0.78%. By comparison, Massachusetts birth certificates for the same period yielded an average congenital malformation rate of 1.33%. These figures should be compared only to each other, but not to national rates and those from specified studies, all of which include anomalies reported after birth certificates are filed. Data on congenital anomalies for 1982 are not yet available for Plymouth or Massachusetts.

Fetal deaths: A high fetal death rate can be considered an indicator of poor pregnancy outcome. A fetal death refers to a death prior to the complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of pregnancy. The death is indicated by the fact that after such separation the fetus does not breathe or show any other evidence of life, such as the beating of the heart, pulsation of the umbilical cord, or definite movement of the voluntary muscles.

In Massachusetts, all fetal deaths of 20 or more weeks gestation or greater than 350 grams must be reported. An analysis of these reported deaths shows that the rate of fetal deaths in Plymouth is consistently lower than that of Massachusetts except for 1979. (Figure V-2). In 1979, the rates are similar (6.7% for Plymouth and 6.0% for Massachusetts). In addition, for 1978 and 1980 the rates are extremely low. It is impossible to determine why 1978 is so low, 1979 equal to Massachusetts, and 1980 much lower except to say that the real numbers are extremely small and that statistically, the peak in 1979 is insignificant.

FIGURE V-2.
FETAL DEATH RATE IN PLYMOUTH AND MASSACHUSETTS
1975 - 1981



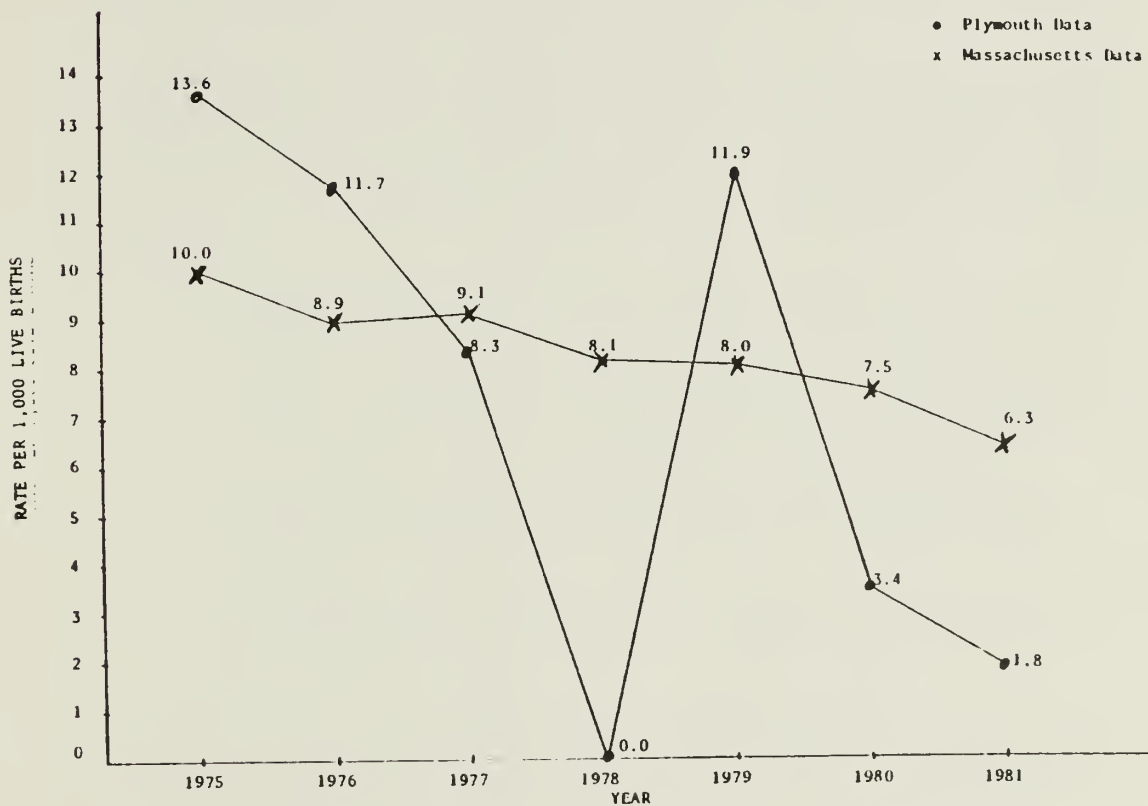
Massachusetts Department of Public Health, Vital Statistics, Fetal Death Certificates

Neonatal mortality: An important indicator of pregnancy outcome is neonatal mortality. As knowledge about reproduction and the factors which influence outcome has increased and improvements in health care have occurred, there has been a significant decline in neonatal mortality over the past ten years. Thus, the finding of a consistent increase in neonatal mortality over two or more years could indicate potential health service problems, environmental agents, or new maternal/fetal problems.

An analysis of the Plymouth neonatal mortality rate (Figure V-3) compared to that of the state indicates a sharp decline from 1975 to 1978 followed by a one-year increase in 1979. Following 1979, the rates again decline precipitously. Thus, there is no evidence that the neonatal mortality rate for Plymouth exceeds that for the Commonwealth as a whole.

FIGURE V-3.

NEONATAL MORTALITY RATE PER 1,000 LIVE BIRTHS IN
PLYMOUTH AND MASSACHUSETTS (1975 - 1981)



The data for the neonatal deaths in 1979 were carefully reviewed. Seven deaths occurred. six were infants of less than 27 weeks gestation (including one set of twins), or the result of medical complications of pregnancy. Only one was related to a congenital anomaly. The deaths were spaced throughout the year and were geographically disparate. It was impossible to determine any association between specific cases. Statistically, the one-year increase can be explained due to the small numbers involved and the low rates for 1978 and 1980.

VI. CHILD HEALTH AT INDIAN BROOK ELEMENTARY SCHOOL

Reports from parents and teachers suggested that children attending IBES were experiencing an unusually high number of headaches, dizziness, nausea, and respiratory symptoms. The approach to addressing this problem was to compare the rates of childhood illness at IBES with those at other school buildings.

METHODS

Absenteeism: In order to explore whether children attending IBES suffer from poorer health than their peers, attendance data from all Plymouth elementary schools since 1979 were analyzed. Comparable elementary school data were obtained for 1980-81 and 1981-82 from two nearby school systems, Brockton and Quincy.* Because of differences in the student population at different buildings, rates of absenteeism were analyzed rather than total child days absent.

Health Room Visits and Dismissals: Rates of health room visits and school dismissals for health reasons were analyzed for the 1981-82 school year. In the Plymouth elementary schools, health rooms are staffed by the school nurse or health aide for most of each day. They maintain detailed daily logs of health room activity.

For this analysis, four months were selected - October, January, March, and June - which represented two low absenteeism and two high absenteeism periods. All recorded visits to the health room except those to receive medication and dismissals were analyzed according to the reason for the visit (complaint). Illness visits relating to the main concern were grouped into two symptom categories. A third group was used for comparison.

- a) Headache/Respiratory: headache, headache and sore throat, cough, "chest hurts", upper respiratory symptoms, dizziness, fainting, asthma attack or wheezing, eye irritation (excluding injury or foreign body), and sore throat; also included in this category are "not feeling well" symptoms, if no further detail was recorded.
- b) Stomach ache/Nausea: stomach ache, nausea, vomiting, retching, stomach ache with headache or with sore throat, diarrhea.
- c) First aid: injuries, accidents, first aid, checks on out-of-school injuries, aches, and pains (if not included under (a) or (b).)

Because this was a Level I investigation, these categories were created to account for differences in the definition and use of the terms headache, nausea, and dizziness. To correct for the effects of irregular health room coverage and student body population and age

*These two systems were chosen because of their geography and demographic similarity to Plymouth, the availability of computerized data, and the number of individual schools in each (giving a perspective on expected differences among schools).

distribution, rates rather than numbers of health room visits were compared. Illness rates were calculated as visits per day per one hundred enrolled students corrected for the period of health room coverage. The Nathaniel Morton School and the Oak Street Kindergarten were excluded from the analysis because they do not serve grades 1-4. Due to time constraints, logs from one new school (Federal Furnace) and one old building (Hedge) were not analyzed.

"Special Consideration" Lists: Each year "special consideration" lists are prepared and maintained by the school nurses. These list by name children with known pre-existing health conditions about which teachers should be aware.* These include bee sting reactions, all types of allergies (food, pollens, drugs, other substances), vision or hearing problems, history of seizures, and other serious medical conditions. These lists are generated from information supplied by parents, from information on physical examination forms, and from experience during the school year. The 1981-82 lists were still available this summer for all buildings when DFHS began its investigation. The lists offered the best Level I view of child health status possible without examining several thousand school health records by hand or asking all parents to submit current health exam reports. The lists for six schools, including the four new buildings, plus Manomet and Hedge Elementary Schools, were reviewed and six categories of problems were generated: 1) headaches; 2) allergies, (excluding those to insects, drugs, or foods, if noted); 3) asthma; 4) hearing or ear problems; 5) vision problems; and 6) "serious medical conditions" (any problem not counted in (1)-(5) which might be serious).

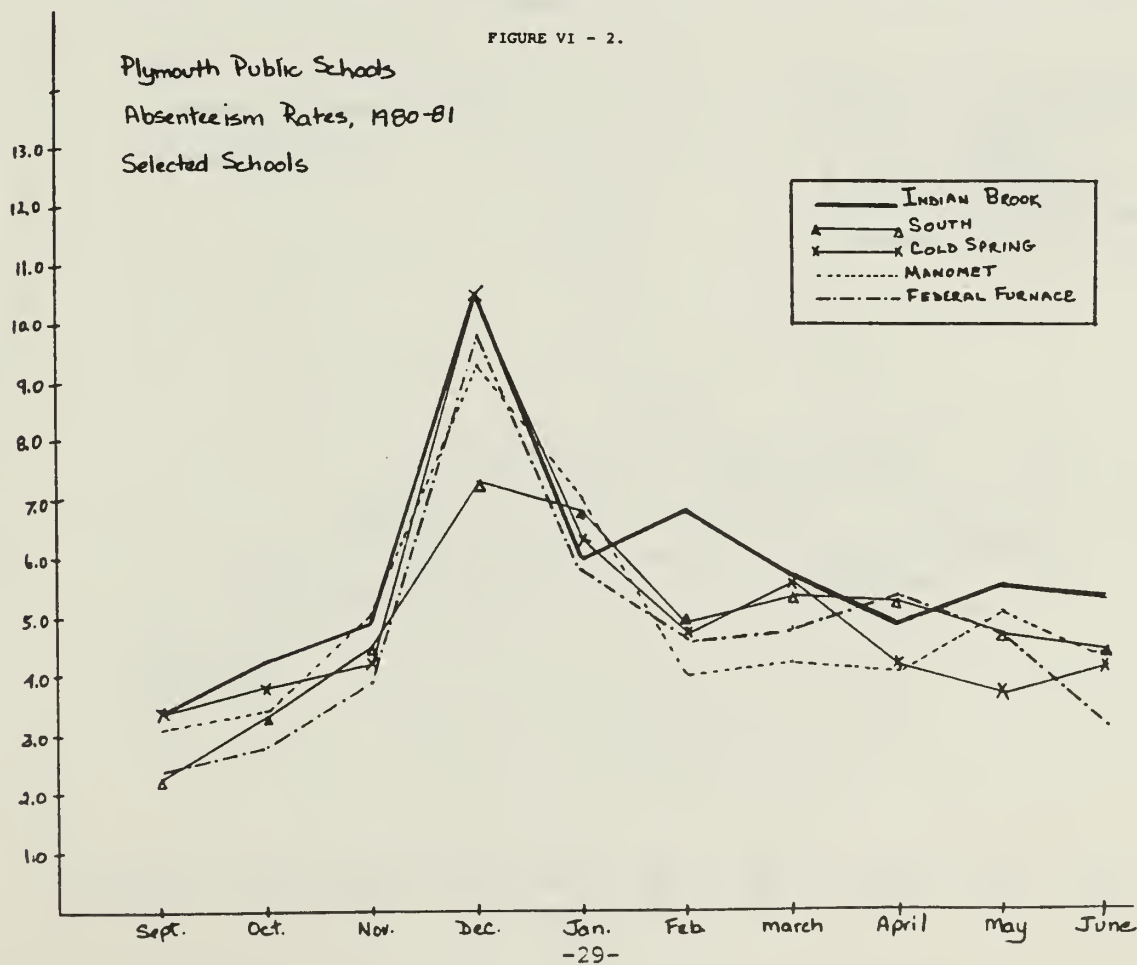
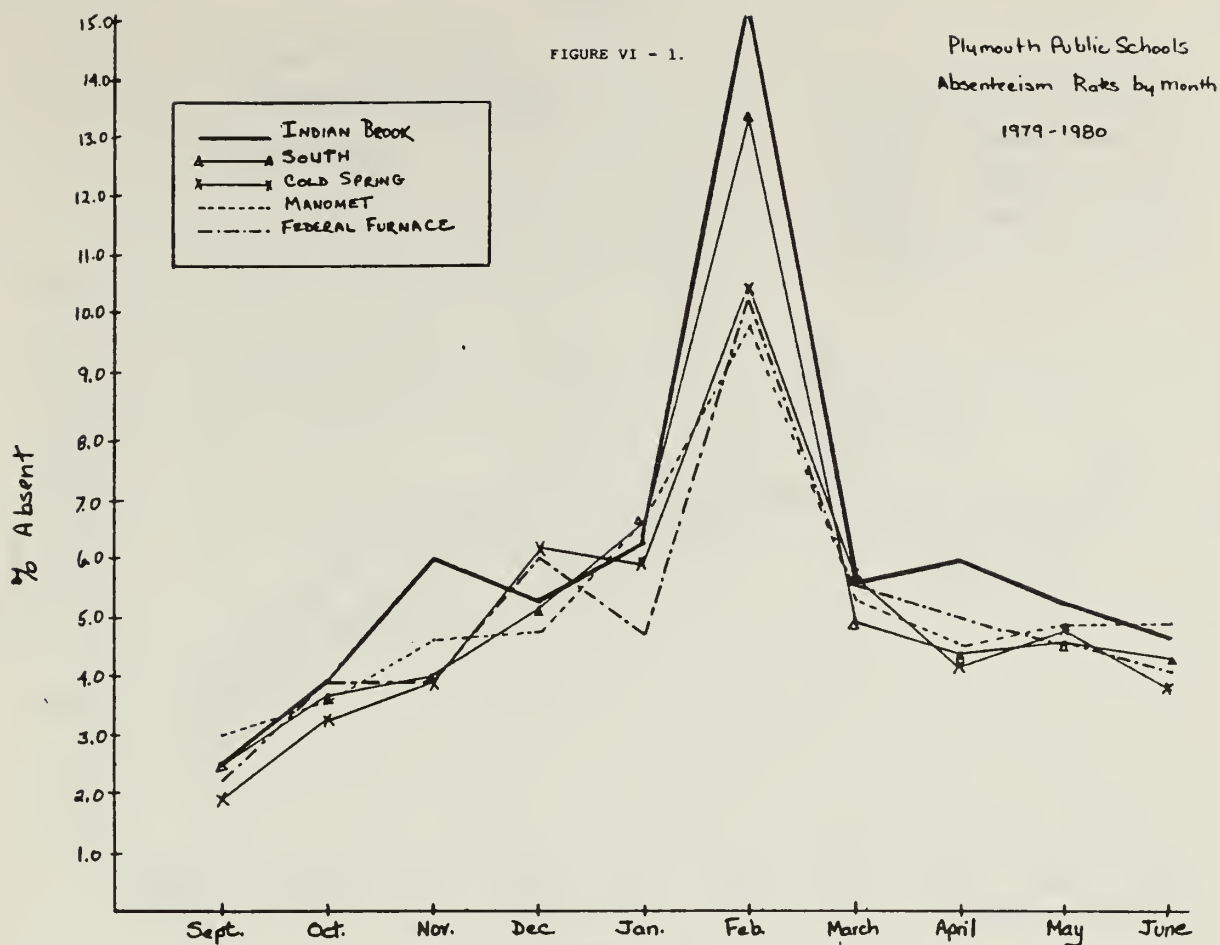
The types of possible statistical analyses were more limited than for other data sets discussed in this report. There are limited data available for comparison either for the state or nation on such variables as absence rates by age or prevalence rates of specific symptoms in health rooms. For these reasons, other elementary school buildings in the Plymouth system served as controls for IBES.

FINDINGS

Absenteeism: Seasonal trends in absenteeism from the IBES shows the same pattern as that from the other elementary schools in Plymouth over a three-year period from 1979 to 1982. This analysis shows that there is no evidence to conclude that children at IBES have a different absenteeism rate from other elementary school children in the town.

During 1979-80 and 1980-81 (Figures VI-1 and VI-2), monthly rates ranged from a low of 1.9% (Cold Spring Elementary School, September 1979) to a high of 15.4% (IBES and Oak Street Kindergarten, February, 1980), with sharp, concurrent peaks in February and December, 1980, possibly representing outbreaks of contagious childhood disease. Absenteeism rates at IBES followed the same pattern as all the other buildings. Among all buildings (not just those graphed), IBES had the highest or tied-for-highest rate only four months out of twenty (versus six months for Nathaniel Morton School and seven for the Hedge School). In 1981-82 (Figures VI-3 and VI-4), absenteeism rates peaked in different months in different elementary schools and were generally lower than those for the preceding two years. The

*These lists are maintained as confidential student records by classroom teachers and are not posted. They are updated throughout the year.



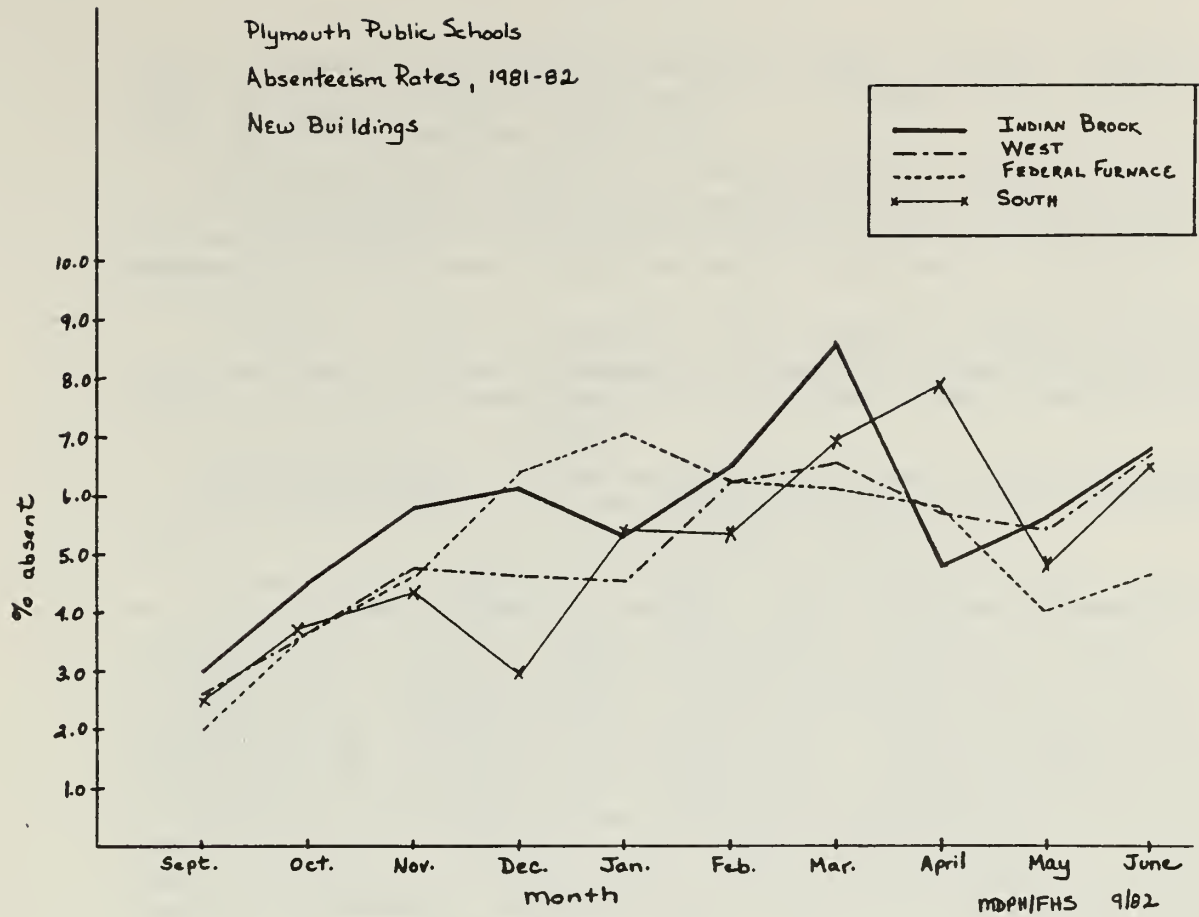
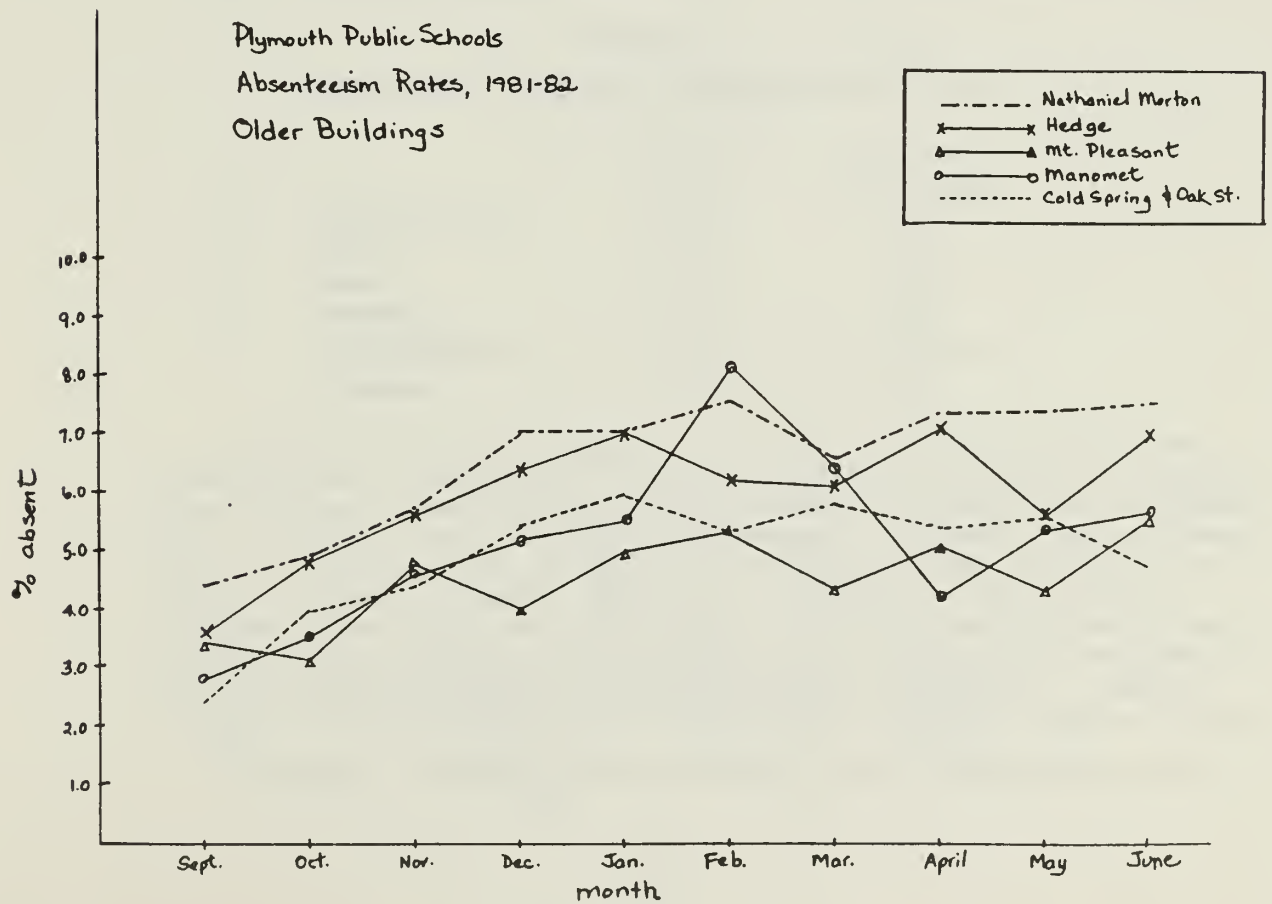


FIGURE VI - 4.



highest absenteeism rate from IBES was 8.6% in March. However, this peak is similar to ones in other winter months at the Manomet, Nathaniel Morton, South, and Hedge elementary schools.

System-wide rates by month for all elementary buildings were compared to those of the Brockton and Quincy elementary schools. While Quincy's rate was consistently low with little variation, Brockton's rates showed seasonal peaks in December, 1980, and March, 1982, similar to those in Plymouth.

In summary, analysis of absentee rates revealed no unexpected patterns among IBES pupils, either in general or for specific months. All of the rates found are approximately equal to national means for elementary schools, five percent per year per student.

Childhood Illness: An examination of health room visit and dismissal data showed that childhood illness rates at IBES did not vary significantly from those at the other four Plymouth schools studied.

During the four months studied at the Indian Brook, Manomet, South, West, and Cold Spring Elementary Schools, 4,467 visits were recorded to the five health rooms; and 502 children were dismissed for health reasons. This represents a total of 386 health room days (an average of 19.3 days of coverage per building per month). The average visit rate for the four schools was 2.23 visits per 100 children per day and .24 dismissals per 100 children per day for the four months studied. These visit and dismissal rates (Table VI-1) appear typical for elementary schools. For visits, IBES at 1.94 falls in the middle of the range, with Manomet highest at 3.85 and West lowest at 1.27. For dismissals, IBES at 0.31 again falls in the range created by Manomet as highest at 0.33 and West lowest at 0.09. In summary, there are no systematic differences between IBES and other Plymouth schools in visit or dismissal rates.

TABLE VI-1
HEALTH ROOM VISIT AND DISMISSAL RATES, 1981-82
Per 100 Students

	<u>Visits</u>	<u>Dismissals</u>
Indian Brook	1.94	.31
South	2.60	.22
West	1.27	.09
Manomet	3.85	.33
<u>Cold Spring</u>	<u>1.47</u>	<u>.27</u>
Average	2.23	.24

Figures VI-5 and VI-6 display the data on the number of visits and dismissals per 100 enrollment for the five schools during the four specific months studied. There is some pattern visible, with West School consistently having the lowest rates of visits and dismissals. However, IBES is almost always intermediate, with the exception of high dismissal (but not visit) rates for October and March. There is no evidence for any systematic difference between IBES and the other schools. A further analysis of health room visit and dismissal rates according to the symptom groups described earlier (headache/respiratory, stomach/nausea, and first aid), showed similar variations by month, with IBES in no way presenting a unique profile.

In summary, our analysis of retrospective data on health room visits

FIGURE VI-5
HEALTH ROOM VISITS PER DAY PER 100 ENROLLED STUDENTS
1981-82

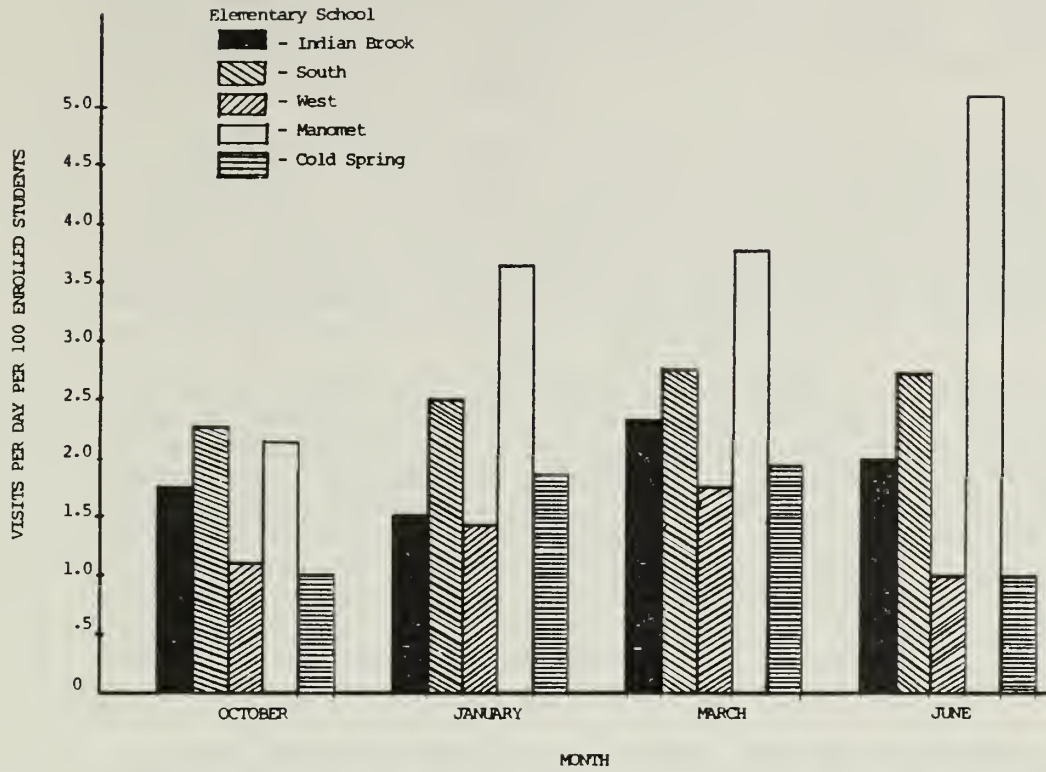
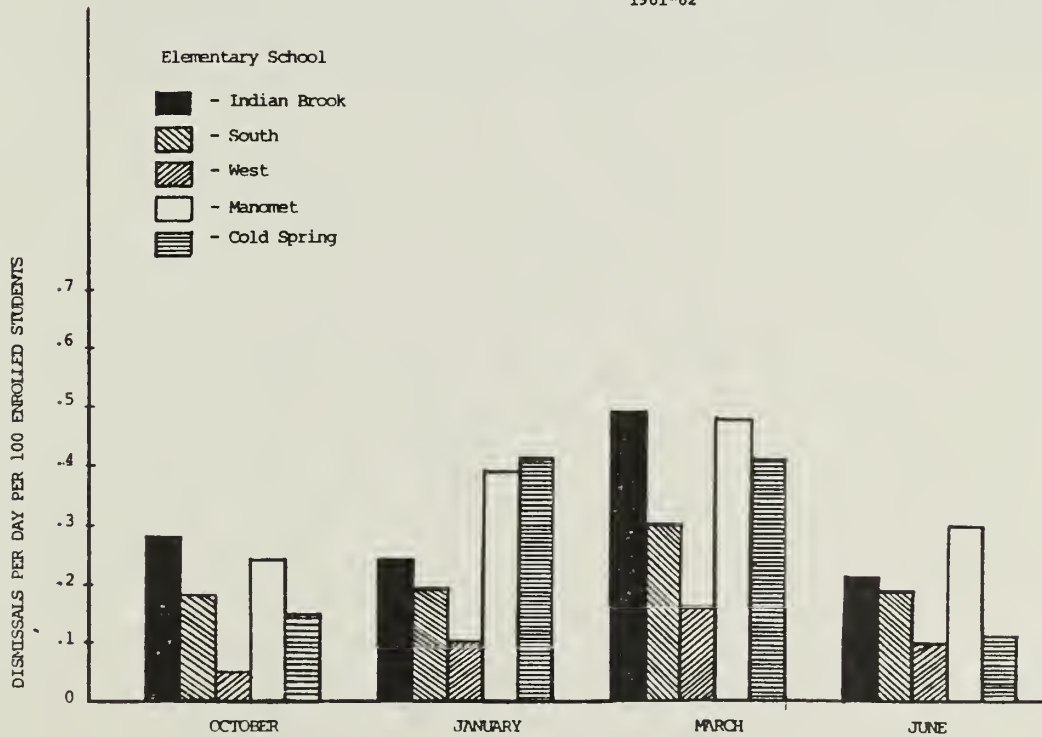


FIGURE VI-6
DISMISSALS PER DAY PER 100 ENROLLED STUDENTS
1981-82



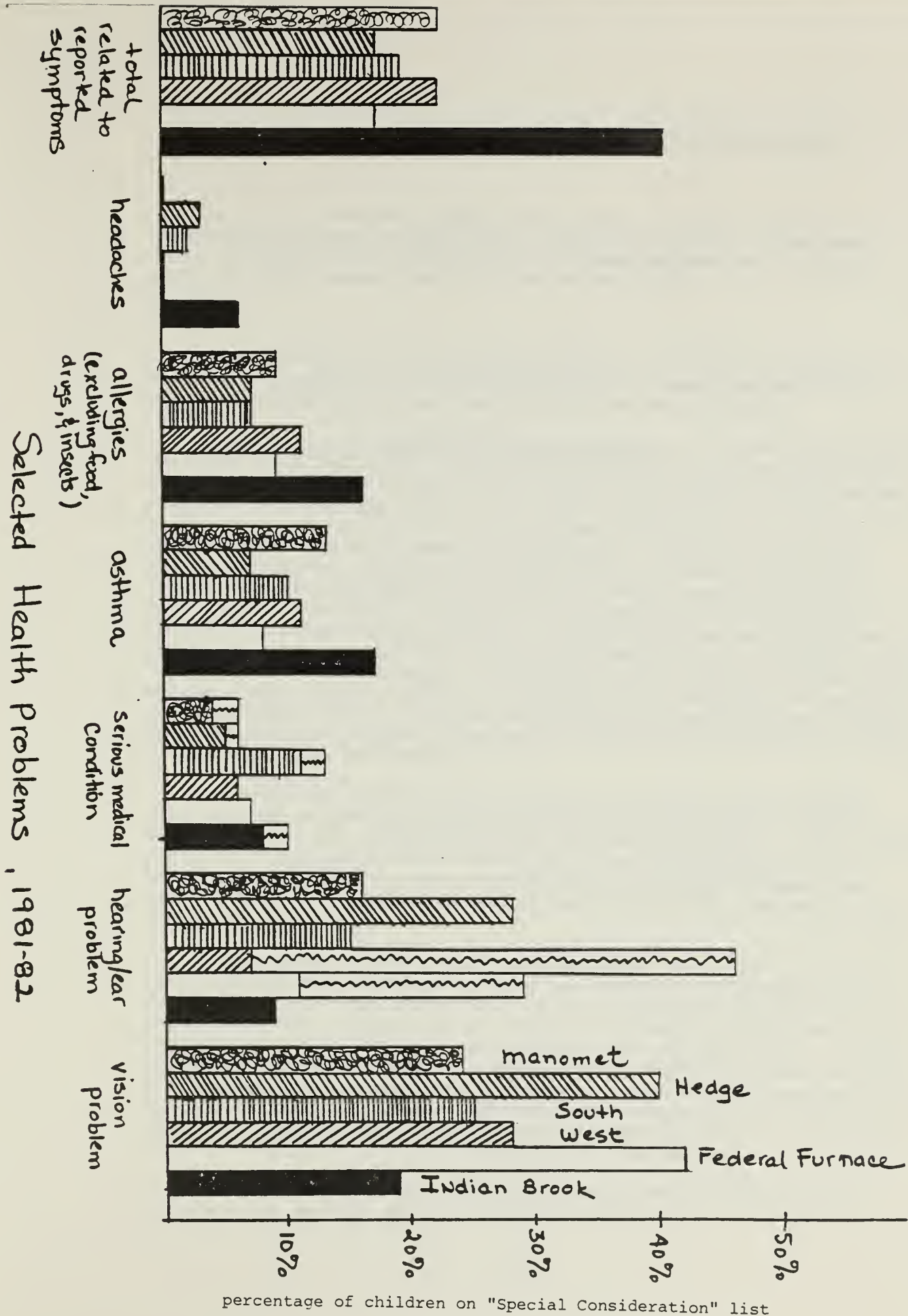
and dismissals for health reasons in 1981-82 reveals no elevated risk or adverse experience for children attending IBES. In fact, there really are more complaints, as would be indicated by the parents' reports, then the school nurses are not aware of them because these complaints have not been brought to their attention.

Figure VI-7 displays data from the six schools regarding the percentage of all children on the "special consideration" lists having each of the six problems. If a child had problems in more than one category, each was counted. The first three categories are potentially related to the types of health problems reported by parents of IBES students. Thus, each category is shown separately, but they are also combined into a composite "related to reported symptoms" category (far left set of bars).

This analysis reveals the only difference between IBES students and those at the four other elementary schools. Thirty-nine percent of IBES students had one or more of the complaints listed. Rates at the other schools ranged between 17% and 22%. It is impossible to determine whether children named on these lists had these conditions before entering IBES or were added to the list due to complaints that occurred while at the school. The data permit us to speculate that possible exposure to a poorly ventilated and underheated facility may have exacerbated problems in children with increased susceptibility. If this is the case, the changing of the ventilation configurations at the school should result in relief from many of the symptoms reported by parents.

This finding, however, is of limited significance because there is no evidence from the actual health room logs of an increase in complaints of headaches and respiratory problems. This lack of evidence cannot be blamed on recorder bias since both the Manomet and South schools, which have lower percentages of children with related problems and comparable visit rates, are staffed by the same nurse and aides. An improved reporting system now in use may assist in identifying true differences among the groups of students and their health room use in the future.

FIGURE VI - 7.



VII. REPRODUCTIVE OUTCOMES AT INDIAN BROOK ELEMENTARY SCHOOL

In order to determine whether there was an increase in adverse reproductive outcomes at IBES and to test whether working at the school was a reproductive risk factor, Level II investigations were conducted among all staff members who have ever worked at IBES.

METHODS

Because female and male reproduction are so differently affected by environmental exposures and because there were so many more IBES female staff, different methods were used to study the men and women.

Investigation of female reproductive outcomes: A lengthy questionnaire, developed specifically for this Level II study, was administered by DFHS staff to 94 women who represent 84% of the 112 women who have ever worked at IBES. The remainder couldn't be reached, preferred not to participate, or were over 52. The objective of the interview was threefold. First, a complete catalogue of outcomes was established: normal births, births with birth defects, miscarriages, stillbirths, and elective abortions. Second, data were gathered on nine factors, called covariables, which might explain the group's reproductive outcomes based on known medical information: mother's age, gravidity, contraceptive method, medications during pregnancy, alcohol use in pregnancy, smoking during pregnancy, other maternal medical conditions, and prior reproductive history, and labor and delivery complications. Third, the timing of each conception and gestation was established; those conceptions and gestations occurring before or after IBES employment are labeled "unexposed"; those occurring during the period of IBES employment are "exposed."

The method of analysis was as follows: For each outcome category, rates were calculated for unexposed and exposed pregnancies. The data were stratified into categories within the nine covariables. Mantel-Haenzel statistics (rate ratios) were calculated to test for confounding. In non-technical terms, all cases were divided into covariable categories. Each category was tested to uncover any associations that factors in other categories might hide or produce.

Investigation of male reproductive outcomes: Both Level I and Level II investigations were conducted to study male reproductive outcomes. A questionnaire was administered to 27 of the 36 men who have ever worked at IBES (75%). The remainder either could not be reached or preferred not to participate. The objective of the interview was threefold: 1) a catalogue of outcomes was established, 2) identify other factors that might explain poor reproductive outcomes; and 3) determine timing of each pregnancy outcome to exposure to IBES. However, because of small sample size and very limited scientific knowledge about factors affecting male reproductive outcome, we could not reasonably control for confounding covariables.

Consideration had been given to eliminating men at special risk for poor outcomes from the analysis. These would be men who had either a

medical condition or exposure to an agent known to affect reproductive outcome. Two such men were found. However, because the danger of exposure to their particular risk factor rests on very weak scientific ground and because their exposures were far in the past, they were retained in the analysis.

Because of the small number of pregnancies reported, odds ratios were not calculated. Instead, the method of analysis was to compare individual outcome categories in IBES-exposed pregnancies to national norms.

FINDINGS

Reproductive outcomes in female employees: Analysis revealed no evidence to conclude that adverse reproductive outcomes could be attributed to IBES exposure, after controlling for known confounding risk factors. During the investigation, 189 pregnancies were identified; these constitute the units of analysis or "cases."

Table VII-1 contains the overall results. First, a technical description of the findings will be given. A non-technical interpretation follows.

Working at IBES did not increase this group's risk of adverse reproductive outcomes, even corrected for the effects of the covariables. For the odds ratios over 1.00, the 95% confidence interval always includes 1.00. (A 95% confidence interval which includes 1.00 is not statistically significant by chi-square testing at $p < 0.05$ level.)

For every covariable, the adjusted odds ratio was within 15% of the crude (or unadjusted) ratio, which means that stratification did not uncover any hidden associations. Additionally, the adjusted odds ratios all fell outside the range of statistical significance, confirming the results of Table VII-1.

In non-technical terms, Table VII-1 shows that among the 94 women studied, 189 pregnancies occurred. Of these, 167 occurred prior to the woman's employment; 22 occurred during employment. In total, 164 pregnancies resulted in live births. There were no neonatal deaths among the exposed group. Therefore, no statistical evaluation could be made here. For miscarriages, 20 occurred among the 167 unexposed pregnancies and 3 among the 22 exposed pregnancies. There is virtually no statistical probability that exposure to IBES resulted in increased miscarriage rates. There was only 1 stillbirth in each exposure category, and one can have very little confidence in any analysis that describes the difference between these groups.

In response to concern that all the miscarriages occurred in a short period of time, this investigation included a detailed examination of these three pregnancies. There is no way to explain this occurrence. However, one miscarriage occurred in a medically high risk pregnancy. The other two occurred in pregnancies which showed no risk factors in their medical histories or gestation. Due to the high probability of two common events occurring at the same time by chance and due to the inability to measure or detect an exposure that might have occurred in the past, there is no scientific way to link these miscarriages or to determine their causes, whether environmental or otherwise.

TABLE VII-1.

FREQUENCIES AND ODDS RATIOS OF FEMALE PREGNANCY OUTCOMES, IBES

IBES EXPOSURE

<u>Outcome</u>	<u>Unexposed</u>	<u>Exposed</u>	<u>Odds Ratio</u>	<u>95% Confidence Interval</u>
All Pregnancies	167	22	NA	NA
Live Births	146	18	1.0 (Referrent)	NA
No Birth Defects	132	15	NA	NA
Birth Defects	14	3*	1.7	(0.54 - 5.60)
Neonatal Deaths	3	0	- **	
Conceptus Deaths	21	4	1.5	(0.54 - 3.90)
Miscarriage	20	3	1.2	(0.38 - 3.70)
Stillbirth	1	1	8.0**	(0.8 - 82.6)
All Poor Outcomes	38	7	1.4	(0.69 - 2.82)

NA = Not applicable; refers to the reference and good outcomes (not being studied).

* The number of birth defects included is smaller than the number reported publicly. Two cases were excluded from the analysis. Upon close clinical review of these cases, it was determined that they cannot be considered birth defects.

** No odds ratio can be calculated if one of the frequencies is a zero. If one of the frequencies is "1", an odds ratio can be calculated but has little meaning.

Birth defects occurred 1.7 times as frequently in IBES exposed pregnancies than in non-exposed pregnancies. However, the statistical methods available to assess these data indicate that this difference is not statistically significant. Because the number of cases is small and the expected frequency of the event is relatively high, the difference in the rates of birth defects can be attributed to a random distribution of events, in other words, to chance.

Sterility was evaluated separately. "Sterility" is defined as failure to conceive after twelve months of sexual intercourse without contraception. (This definition is very liberal; most authorities suggest two years of regular intercourse. Therefore, the number of reportedly sterile women in this study is probably high.) Fifteen women were found who were sterile according to this definition. Of these, twelve consulted a physician for this condition.

In ten of these twelve women, (1) the period of documented sterility occurred either completely or partially prior to their employment at IBES or (2) their husband had a documented medical problem that would account for the failure to conceive. Of the remaining two women who consulted a physician, both failed to conceive during IBES exposure. However, one of these women had a documented medical condition to account for her problem. Therefore, there is only one woman who had an unexplained period of sterility since starting at IBES. No statistical statement can be made about this single case.

Three of the fifteen women did not consult a physician for their problem. Usually, without information from a medical examination, it is impossible to speculate about the possible causes of sterility in an individual. Since, in all three cases, the periods of sterility occurred or began prior to employment at IBES, it would appear, nevertheless, that exposure to IBES is not associated with these three cases.

Reproductive outcomes in male employees: There were 44 reported pregnancies fathered by IBES staff (Table VII-2.). In no case did the difference between observed and expected number of outcomes even approach statistical significance. In other words, there was no detectable association found between IBES exposure and poor reproductive outcome for male employees as a group, including sterility. Two qualifications need to be made. First, the sample size lacks the power to detect anything but the very largest increase in risks. Second, when the numbers are so small, any error in reported or random fluctuation in events is greatly magnified.

TABLE VII-2.

FREQUENCIES OF MALE REPRODUCTIVE OUTCOMES, IBES

IBES EMPLOYEES					
<u>Outcome</u>	<u>USA</u>	<u>Unexposed</u>	<u>Exposed</u>		<u>P Value</u>
		<u>Observed</u>	<u>Observed</u>	<u>Expected*</u>	
Live Births		35	5		
No Birth Defects		32	5		
Birth Defects	3%-5% (of live births)	3	0	0.2	NA
Neonatal Deaths		0	0		
Conceptus Deaths	17%-29% (of pregnancies)	2	1	1.2	>0.10
Miscarriage	15%-25% (of pregnancies)	1	1	1.2	>0.10
Stillbirth	2%-4% (of stillbirth and livebirths)	1	0	0.1	NA
All Outcomes		37	6		
All Poor Outcomes	20%-34% (of pregnancies)	5	2	1.4	>0.10
Sterility		2	1	0.7	>0.10

NA = Not Applicable; applies to those cases where fewer cases were observed than expected.

* Calculated using lowest value of USA percentage.

VIII. SUMMARY AND RECOMMENDATIONS

In July, 1982, the Division of Family Health Services (DFHS), Massachusetts Department of Public Health, joined other State, Federal, and private agencies in investigating concerns about apparent health problems among teachers and pupils at the Indian Brook Elementary School (IBES). DFHS assumed responsibility for investigating whether or not reported levels of childhood illness and poor reproductive outcomes, such as miscarriages, stillbirths, and birth defects, were higher than would be expected. Other agencies including the Massachusetts Division of Environmental Health Assessment, the Massachusetts Department of Environmental Quality Engineering (DEQE), the Division of Occupational Hygiene, the National Institute of Occupational Safety and Health (NIOSH), and a private consulting firm (Toxicon Associates) assumed responsibility for the investigation of hazardous substances in the school.

The overall goal of the investigation was to determine whether or not there was an unusually high level of health problems among the pupils and staff of the school and whether these health effects could then be linked to any environmental hazards found at the IBES.

The epidemiologic investigation conducted by DFHS began with a Level I review of available data on illness among pupils at IBES, the status of child and reproductive health in Plymouth, and childhood cancers at IBES and Plymouth. Then a detailed Level II survey investigation was undertaken to specifically investigate reproductive health among all male and female employees who had worked at IBES since its opening in 1977. Both technical (statistically precise) and non-technical explanations of the methods and analyses used are included in the methods section of the report.

The findings of the study are grouped into three categories: health status indicators for Plymouth, child health at IBES, and reproductive outcomes at IBES. In addition, the environmental findings of other agencies are reviewed.

In summary, an examination of infant mortality, childhood deaths by various causes, and childhood cancers since 1975 showed that Plymouth has no more of these child health problems than would be expected for the Commonwealth as a whole. In particular, a careful search for childhood cancers using all available sources and community reports showed no significant levels of excess cancer. Among the available measures of reproductive outcome reviewed for the Town of Plymouth were congenital anomalies, neonatal mortality, and fetal deaths. Again, the observed rates for these outcome indicators for Plymouth for the period 1975-1981 were as good as, if not better, than the State average.

Child health at IBES was examined by reviewing school information on absenteeism, health room visits and dismissals, and lists of children with special health conditions. The children of IBES were compared to those attending other schools in Plymouth. The data also were checked against comparable data from school systems in Brockton and Quincy.

Absenteeism at IBES was no different from that at other elementary schools with a strong pattern of seasonal peaks during the winter months. In the Winter of 1982, the peak absentee month was March, but absenteeism occurred at a lower level than in previous years. Dismissals from school also had a seasonal pattern with a winter peak, but again, IBES was not significantly different from the other schools.

The review of the lists of children with health problems of "special consideration" does show some differences between the IBES and other elementary schools, an apparently higher prevalence of problems related to the symptoms reported by the community. These data suggest that exposure to a poorly ventilated and underheated facility may have exacerbated problems in children with increased susceptibility. While one must be cautious with the interpretation of these data, it seems that the observations of IBES parents that their children were having more respiratory illness and other symptoms may be corroborated.

In order to determine whether there was an increase in adverse reproductive outcomes among staff at IBES, detailed reproductive history questionnaires were administered to 94 of the 112 women and 27 of the 36 men who had worked at the school. Among the women, 189 pregnancies were identified of which 22 occurred during the period of employment at IBES. Analysis for birth defects, miscarriages, and stillbirths revealed no statistically significant increase in these adverse reproductive outcomes that could be attributed to IBES. The clustering of 3 miscarriages in the Spring of 1982 could not be explained; but there were clinical grounds to believe that at least one of these occurred in a medically high risk pregnancy. All conclusions must be qualified in light of the small number of individuals available for study. Among the small number of pregnancies fathered by men who worked at the IBES, there was no evidence of increased poor reproductive outcomes or sterility. Again, the number of individuals available for study resulted in a study of low power and less reliable findings.

These epidemiologic findings must be viewed in the light of the environmental studies carried out at IBES by various agencies. These studies found that ventilation of the building was extremely poor during the heating season, permitting the build-up of common pollutants, including formaldehyde. In addition, a high level of methanol was found in the teachers' lounge where the duplicating machines were located.

Conclusions:

In conclusion, we believe that there is some evidence that may link increased childhood respiratory and related symptoms in children, who already may be susceptible, in a poorly ventilated building where common pollutants and irritants could build up, particularly in winter. No direct relationship can be established retrospectively, but the policy implications for improving building ventilation are clear.

There is no convincing evidence, however, that an increase in poor reproductive outcomes has occurred among staff at IBES. This conclusion must be qualified by the caution that the study is biologically and statistically limited by the small number of individuals involved. Furthermore, there is

no literature that links methanol or formaldehyde exposure to adverse reproductive outcomes; and no such evidence was found here.

In conclusion, there is no evidence that Plymouth has more childhood illness, poor reproductive outcomes, or childhood cancer than the rest of Massachusetts. Despite the limitations inherent in the study, the Division feels that the investigation has been conducted with thoroughness and that the community should feel reassured about the safety of the Indian Brook Elementary School.

Recommendations:

1. The Indian Brook Elementary School should be reopened with modifications of the heating, ventilation and air conditioning systems as recommended by the environmental consultants. Environmental monitoring of the schools should be continued.
2. While no special health studies of the school children should be started, school nurses and health aides in all the schools built for energy efficiency should continue to monitor child health and absenteeism and review these data regularly for evidence of patterns of illness.
3. While no Level III monitoring system should be established at this time, the Board of Health should continue to monitor health status indicators, reproductive outcome factors, and cancer cases for the Town of Plymouth and its schools.
4. Staff members and families of children at IBES should be informed about the results of the studies to date and reassured of the safety of the school. The school committee should consider setting up a special information program for IBES to allay any fears or confusions that have arisen.

